

Remarks

Priority Claims

This application is a divisional of 09/880,141 filed June 13, 2001, which is a divisional of Application No.08/836,670 filed May 22, 1997, now US patent 6,300,335. The priority of each of the aforementioned applications under 35 USC §120 is hereby claimed by Applicants.

The grandparent application was filed based on PCT/EP95/04066. Applicants also claim the priority of that PCT application.

The above-mentioned PCT application was filed claiming priority to UK provisional application UK 9423910.0. Applicants, under 35 USC §119, also claim the priority of that UK application.

The Instant Divisional

In the instant divisional application, Applicants have elected to prosecute a method for treating erectile dysfunction in a male animal, comprising administering to an animal in need of said treatment an effective amount of a pyrazolopyrimidine as disclosed in European patent application 0636626. This corresponds to group xxv disclosed in predecessor (grandparent) application 08/836,670. Group xxv was not restricted out of the grandparent application in the Office Action of October 8, 1997, although it is believed this was an oversight. Group xxv was originally claimed in claim 5 of that application.

Applicants have attempted to place the instant application into the same format the parent was in when it was allowed.

A copy of the parent application for prosecution in the instant (divisional) application has been provided along with the filing papers for this application, plus a copy of the declaration filed in the parent. It is noted that the application copy is a copy of the international application, PCT/EP95/04066, which designated the United States, and which was published as WO 96/16644.

A marked-up and a clean substitute specification, in addition to the copy

of the parent application, are each also enclosed with this preliminary amendment. Matter which has been reproduced and/or transferred from EP 0636626 has been underlined in the markup as required by the new revised amendment practice. Matter which has been reproduced and/or transferred from EP 0636626 is, generally, as follows:

1. A sentence updating the status of the present application as a divisional application of application no. 09/880,141, which is a divisional application of application no. 08/836,670 filed May 22, 1997, now US Patent 6,300,335 which is a National Phase filing under 35 USC §371 based on PCT/EP95/04066 which was filed internationally on 16 October 1995 and which was published internationally as WO 96/16644 on 6 June 1996.

2. A transitional sentence which introduces the reader to the fact that the application is switching to a new specific subject, namely the above-mentioned EP 0636626.

3. A closing sentence referring the reader to the European Application for further information.

4. A word added as the first word in the abstract to identify the types of compounds in the instant application more precisely.

It is noted that certain material in the original specification (i.e., in the title and the abstract) was underlined as part of the original write-up. This underlining has been removed in order to facilitate identification of the textual material that has been added to the instant marked up substitute specification.

The text transferred from EP 0636626 to the substitute specification has been tacked on to the end of the original specification. The Claims and Abstract, as originally filed, also form a portion of the substitute specification. The claims and the Abstract are as originally filed except as noted above. As mentioned above, all transferred text has been underlined in accordance with revised amendment practice.

The undersigned hereby states that the substitute specification accompanying this Amendment and Response contains no new matter.

Amendments to the Instant Application

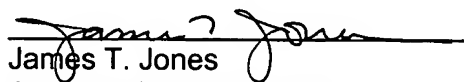
The text of EP 0636626, page 3 from line 7 to 55 (except for adapting some introductory words at the beginning and deleting the words "for use in therapy" at the end) has, by amendment, been reproduced in newly added claim 8.

Original claims 1 through 7 have been canceled.

It is believed that the Examiner will find the substitute specification satisfactory in all respects. It is not seen that there are any issues outstanding to be resolved in this application. Accordingly, a Notice of Allowance is respectfully requested.

Respectfully submitted,

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MARKUP SUBSTITUTE SPECIFICATION**cGMP-PDE INHIBITORS FOR THE
TREATMENT OF ERECTILE DYSFUNCTION**

This is a divisional application of application no. 09/880,141, which is a divisional application of application no. 08/836,670 filed May 22, 1997, now US Patent 6,300,335 which is a National Phase filing under 35 USC §371 based on PCT/EP95/04066 which was filed internationally on 16 October 1995 and which was published internationally as WO 96/16644 on 6 June 1996.

This invention relates to the use of compounds which are selective inhibitors of cyclic guanosine 3',5'-monophosphate phosphodiesterases (cGMP PDEs) in the treatment of erectile dysfunction (impotence) in male animals, including man.

Impotence can be defined literally as a lack of power, in the male, to copulate and may involve an inability to achieve penile erection or ejaculation, or both. More specifically, erectile impotence or dysfunction may be defined as an inability to obtain or sustain an erection adequate for intercourse. Its prevalence is claimed to be between 2 and 7% of the human male population, increasing with age, up to 50 years, and between 18 and 75% between 55 and 80 years of age. In the USA alone, for example, it has been estimated that there are up to 10 million impotent males, with the majority suffering from problems of organic rather than of psychogenic origin.

Reports of well-controlled clinical trials in man are few and the efficacy of orally administered drugs is low. Although many different drugs have been shown to induce penile erection, they are only effective after direct injection into the penis, e.g. intraurethrally or intracavernosally (i.c.), and are not approved for erectile dysfunction. Current medical treatment is based on the i.c. injection of vasoactive substances and good results have been claimed with phenoxybenzamine, phentolamine, papaverine and prostaglandin E₁, either alone or in combination; however, pain, priapism and fibrosis of the penis are associated with the i.c. administration of some of these agents. Potassium channel openers (KCO) and vasoactive intestinal polypeptide (VIP) have also been shown to be active i.c., but cost and stability issues could limit development

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of the latter. An alternative to the i.c. route is the use of glyceryl trinitrate (GTN) patches applied to the penis, which has been shown to be effective but produces side-effects in both patient and partner.

As a general alternative to pharmacological intervention, a variety of penile prostheses has been used to assist achievement of an erection. The short term success rate is good, but problems with infection and ischaemia, especially in diabetic men, make this type of treatment a final option rather than first-line therapy.

According to the specification of our International patent application no PCT/EP94/01580, (publication no WO94/28902), we describe and claim the use of a series of pyrazolo [4,3-d]pyrimidin-7-ones for the treatment of impotence. The compounds are potent and selective inhibitors of cGMP PDE in contrast to their inhibition of cyclic adenosine 3',5'-monophosphate phosphodiesterases (cAMP PDEs). This selective enzyme inhibition leads to elevated cGMP levels which, in turn, provides the basis for the utilities previously disclosed for the compounds in the treatment of stable, unstable and variant (Prinzmetal) angina, hypertension, pulmonary hypertension, congestive heart failure, atherosclerosis, conditions of reduced blood vessel patency, peripheral vascular disease, stroke, bronchitis, allergic asthma, chronic asthma, allergic rhinitis, glaucoma, and diseases characterised by disorders of gut motility, e.g. irritable bowel syndrome. The specification goes on to describe investigations which identified three PDE isoenzymes in human corpus cavernosum tissue, relaxation of which leads to penile erection. The predominant enzyme was found to be the cGMP-specific PDE_v, while cGMP-stimulated cAMP PDE_{ii} and cGMP-inhibited cAMP PDE_{iii}, were also present. The compounds described were found to be potent and selective inhibitors of the PDE_v enzyme but demonstrated only weak inhibitory activity against the PDE_{ii} and PDE_{iii} enzymes. This activity is believed to be responsible for the action of the compounds in the treatment of erectile dysfunction.

A number of cGMP-PDE inhibitors have previously been described in the literature for a variety of utilities, these include use in treating obstructive lung diseases such as asthma and bronchitis, in combatting allergic diseases such as allergic asthma, allergic rhinitis, urticaria, and irritable bowel syndrome; and in combatting angina, hypertension and congestive heart failure. Utility has also

been claimed as diuretics, as antiinflammatory agents, in the treatment of baldness, for conditions of reduced blood vessel patency, and in glaucoma. However there has not previously been any suggestion that any of these compounds would be of utility in the treatment of erectile dysfunction.

Thus the present invention provides the use of a compound which is a selective cGMP PDE inhibitor for the manufacture of a medicament for the treatment of erectile dysfunction in a male animal, including man, wherein said compound is:

- i a 5-substituted pyrazolo [4,3-d]pyrimidine-7-one as disclosed in European patent application 0201188;
- ii a griseolic acid derivative as disclosed in European patent applications nos 0214708 and 0319050;
- iii a 2-phenylpurinone derivative as disclosed in European patent application 0293063;
- iv a phenylpyridone derivative as disclosed in European patent application 0347027;
- v a fused pyrimidine derivative as disclosed in European patent application 0347146;
- vi a condensed pyrimidine derivative as disclosed in European patent application 0349239;
- vii a pyrimidopyrimidine derivative as disclosed in European patent application 0351058;
- viii a purine compound as disclosed in European patent application 0352960;
- ix a quinazolinone derivative as disclosed in European patent application 0371731;
- x a phenylpyrimidone derivative as disclosed in European patent application 0395328;
- xi an imidazoquinoxalinone derivative or its aza analogue as disclosed in European patent application 0400583;
- xii a phenylpyrimidone derivative as disclosed in European patent application 0400799;
- xiii a phenylpyridone derivative as disclosed in European patent application 0428268;
- xiv a pyrimidopyrimidine derivative as disclosed in European patent 0442204;

- xv a 4-aminoquinazoline derivative as disclosed in European patent application 0579496;
- xvi a 4,5-dihydro-4-oxo-pyrrolo[1,2-a]quinoxaline derivative or its aza analogue as disclosed in European patent application 0584487;
- xvii a polycyclic guanine derivative as disclosed in International patent application WO91/19717;
- xviii a nitrogenous heterocyclic compound as disclosed in International patent application WO93/07124;
- xix a 2-benzyl-polycyclic guanine derivative as disclosed in International patent application WO 94/19351;
- xx a quinazoline derivative as disclosed in US patent 4060615;
- xxi a 6-heterocyclyl pyrazolo [3,4-d]pyrimidin-4-one as disclosed in US patent 5294612;
- xxii a benzimidazole as disclosed in Japanese patent application 5-222000; or
- xxiii a cycloheptimidazole as disclosed in European Journal of Pharmacology, 251, (1994), 1.
- xxiv a N-containing heterocycle as disclosed in International patent application WO94/22855.

The invention includes the use of any compound within the scope of the claims of the patents listed above as well as the particular individual compounds disclosed therein.

Of particular interest for use in the present invention are compounds disclosed in EP 0579496, WO93/07124, US 5294612 and WO94/22855 (xv, xviii, xxi and xxiv above); the compounds of EP 0579496 and WO94/22855 being especially preferred.

Examples of particular and preferred compounds from these patents and publications for use in the present invention include:

- 1,3-dimethyl-5-benzylpyrazolo[4,3-d]pyrimidine-7-one (preparation as described in European patent application 201188, Example 1),
- 2-(2-propoxyphenyl)-6-purinone (preparation as described in European patent application 0293063, Example 1),

6-(2-propoxyphenyl)-1,2-dihydro-2-oxopyridine-3-carboxamide (preparation as described in European patent application 0347027, Example 2),

2-(2-propoxyphenyl)pyrido[2,3-d]pyrimid-4(3H)-one (preparation as described in European patent application 0347146, Example 1),

7-methylthio-4-oxo-2-(2-propoxyphenyl)-3,4-dihydropyrimido[4,5-d]pyrimidine (preparation as described in European patent application 0351058, Example 1),

6-hydroxy-2-(2-propoxyphenyl)pyrimidine-4-carboxamide (preparation as described in European patent application 0395328, Example 15),

1-ethyl-3-methylimidazo[1,5a]quinoxalin-4(5H)-one (preparation as described in European patent application 0400583),

4-phenylmethylamino-6-chloro-2-(1-imidazoloyl)quinazoline (preparation as described in European patent application 0579496, Example 5(c)),

5-ethyl-8-[3-(N-cyclohexyl-N-methylcarbamoyl)-propyloxy]-4,5-dihydro-4-oxo-pyrido[3,2-e]pyrrolo[1,2-a]pyrazine (preparation as described in European patent application 0584487, Example 1),

5'-methyl-3'-(phenylmethyl)-spiro[cyclopentane-1,7'(8'H)-(3'H)-imidazo[2,1-b]purin]4'(5'H)-one (preparation as described in International patent application WO 91/19717, Example 9A3),

1-[6-chloro-4-(3,4-methylenedioxybenzyl)aminoquinazolin-2-yl]piperidine-4-carboxylic acid (preparation as described in International patent application WO93/07124),

(6aR,9aS)-2-(4-trifluoromethylphenyl)methyl-5-methyl-3,4,5,6a,7,8,9,9a-octahydrocyclopent[4,5]imidazo[2,1-b]purin-4-one (preparation as described in International Patent application WO94/19351, Example 14),

1-tert-butyl-3-phenylmethyl-6-(4-pyridyl)pyrazolo[3,4-d]pyrimid-4-one (preparation as described in US patent 5294612, Example 90),

1-cyclopentyl-3-methyl-6-(4-pyridyl)-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimid-4-one, (preparation as described in US patent 5294612, Example 83),

2-butyl-1-(2-chlorobenzyl)6-ethoxycarbonylbenzimidazole (preparation described in Japanese patent application 5-222000),

2-(4-carboxypiperidino)-4-(3,4-methylenedioxybenzyl)amino-6-nitroquinazoline (preparation described in International patent application WO94/22855, Example II),

and 2-phenyl-8-ethoxycycloheptimidazole (KT2-734).

Of particular interest for use in the present invention are the compounds:
 4-phenylmethylamino-6-chloro-2-(1-imidazoloyl)quinazoline (preparation as described in European patent application 0579496, Example 5(c)),
 1-[6-chloro-4-(3,4-methylenedioxybenzyl)aminoquinazolin-2-yl]piperidine-4-carboxylic acid (preparation as described in International patent application WO93/07124),
 (6aR,9aS)-2-(4-trifluoromethylphenyl)methyl-5-methyl-3,4,5,6a,7,8,9,9a-octahydrocyclopent[4,5]imidazo[2,1-b]purin-4-one (preparation as described in International Patent application WO94/19351, Example 14),
 1-tert-butyl-3-phenylmethyl-6-(4-pyridyl)pyrazolo[3,4-d]pyrimid-4-one (preparation as described in US patent 5294612, Example 90),
 1-cyclopentyl-3-methyl-6-(4-pyridyl)-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimid-4-one, as described in US patent 5294612, Example 83), or
 2-(4-carboxypiperidino)-4-(3,4-methylenedioxybenzyl)amino-6-nitroquinazoline (preparation described in International patent application WO94/22855, Example II),

Further cGMP PDE inhibitors for use in the treatment of erectile dysfunction are:

- xxv a pyrazolopyrimidine derivative as disclosed in European patent application 0636626;
- xxvi a 4-aminopyrimidine derivative as disclosed in European patent application 0640599;
- xxvii a imidazoquinazoline derivative as disclosed in International patent application WO95/06648;
- xxviii an anthranilic acid derivative as disclosed in International patent application WO95/18097;
- xxix a 4-aminoquinazoline derivative as disclosed in US patent 5436233;
- xxx a tetracyclic derivative as disclosed in International patent application WO95/19978;
- xxxi a imidazoquinazoline derivative as disclosed in European patent application 0668280; or
- xxxii a quinazoline compound as disclosed in European patent application 0669324.

The compounds may be evaluated as selective inhibitors of cGMP-PDE using any of the methods previously described but in particular their activity against cGMP-PDE_v may be assessed as described in our International patent application PCT/EP94/01580, (WO94/28902).

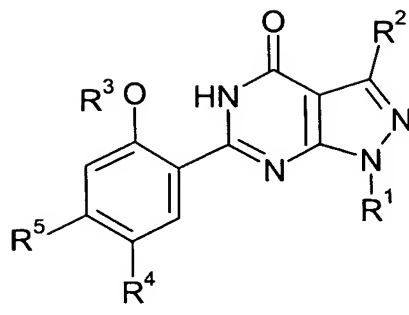
Generally, in man, oral administration is the preferred route, being the most convenient and avoiding the disadvantages associated with i.c. administration. A preferred dosing regimen for a typical man is 5 to 75 mg of compound daily, however the dosage may be increased depending on the potency of the compound being administered and higher dosages are within the scope of the invention. Alternative dosage regimes are also possible depending upon the individual patients circumstances such as the frequency of sexual intercourse. In circumstances where the recipient suffers from a swallowing disorder or from impairment of drug absorption after oral administration, the drug may be administered parenterally, e.g. sublingually or buccally.

For veterinary use, a compound of the invention or a non-toxic salt thereof is administered as a suitably acceptable formulation in accordance with normal veterinary practice and the veterinary surgeon will determine the dosing regimen and route of administration which will be most appropriate for a particular male animal.

Although the compounds of the invention are envisaged primarily for the treatment of erectile dysfunction or male sexual dysfunction, they are also useful for the treatment of female sexual dysfunction including orgasmic dysfunction related to clitoral disturbances, premature labour and dysmenorrhea.

The invention also provides a method of treating erectile dysfunction in a male animal which comprises administering an effective amount of a compound which is a selective cGMP-PDE inhibitor as defined above.

As stated above, one of the groups of compounds of selective cGMP PDE inhibitors is a pyrazolopyrimidine derivative as disclosed in EP 0636626. This document discloses a compound of the formula:



and salts and solvates (e.g. hydrates) thereof, in which:

R¹ represents arylmethyl or C₁₋₆alkyl optionally substituted by one or more fluorine atoms;

R² represents methyl;

R³ represents C₂₋₄alkyl;

R⁴ represents nitro, cyano, C₁₋₆alkoxy, C(=X)NR⁶R⁷, (CH₂)_mNR¹⁰C(=Y)R¹¹ or a 5-membered heterocyclic ring selected from thienyl, thiazolyl and 1,2,4-triazolyl each ring optionally substituted by a C₁₋₄alkyl or aryl group; or when R¹ is arylmethyl or C₁₋₆alkyl substituted by one or more fluorine atoms then R⁴ may also represent hydrogen;

R⁵ represents hydrogen or C₁₋₆alkyl;

R⁶ represents hydrogen or C₁₋₆alkyl;

R⁷ represents hydrogen, amino, hydroxyl, C₁₋₆alkyl, aryl or arylC₁₋₄alkyl;

R⁸ represents hydrogen or C₁₋₆alkyl;

R⁹ represents hydrogen, C₁₋₆alkyl, SO₂R¹², CO₂R¹², C(=NCN)SR¹² or C(=NCN)NR¹³R¹⁴;

R¹⁰ represents hydrogen or C₁₋₆alkyl;

R¹¹ represents C₁₋₆alkyl optionally substituted by one or more halogen atoms, or R¹¹ represents aryl, arylC₁₋₄alkyl, thienyl, NR¹⁵R¹⁶, CH₂NR¹⁷R¹⁸ or R¹⁰ and R¹¹ together represent A(CH₂)_n;

R¹² represents C₁₋₆alkyl, aryl or arylC₁₋₄alkyl;

R¹³ represents hydrogen or C₁₋₆alkyl;

R¹⁴ represents hydrogen, C₁₋₆alkyl, aryl, arylC₁₋₄alkyl or R¹³ and R¹⁴ together with the nitrogen atom to which they are attached form a morpholine, piperazine or N-C₁₋₄alkylpiperazine ring;

R¹⁵ represent hydrogen or C₁₋₆alkyl or R¹⁰ and R¹⁵ together represent – A(CH₂)_n;

R¹⁶ represents hydrogen, C₁₋₆alkyl, aryl, arylC₁₋₄alkyl, CO₂R¹², CH₂CO₂R¹² or R¹⁵ and R¹⁶ together with the nitrogen atom to which they are attached form a morpholine, piperazine or N-C₁₋₄alkylpiperazine ring;

R¹⁷ represents hydrogen or C₁₋₆alkyl;

R¹⁸ represents hydrogen, C₁₋₆alkyl, aryl, arylC₁₋₄alkyl, COR¹² or R¹⁷ and R¹⁸ together with the nitrogen atom to which they are attached form a morpholine, piperazine or N-C₁₋₄alkylpiperazine ring;

A represents CH₂ or C=O;

m represents zero or 1;

n represents 1,2 or 3;

X represents S or NH, or when R7 represents amino then X may also represent

O;

Y represents O or S.

The reader is referred to the original European patent document for a complete discussion and disclosure of syntheses, representative compounds, and so forth, falling within its scope.

CLAIMS

1. The use of a compound which is a selective cGMP PDE inhibitor for the manufacture of a medicament for the treatment of erectile dysfunction in a male animal, including man, wherein said compound is:
 - i a 5-substituted pyrazolo [4,3-d]pyrimidine-7-one as disclosed in European patent application 0201188;
 - ii a griseolic acid derivative as disclosed in European patent applications nos 0214708 and 0319050;
 - iii a 2-phenylpurinone derivative as disclosed in European patent application 0293063;
 - iv a phenylpyridone derivative as disclosed in European patent application 0347027;
 - v a fused pyrimidine derivative as disclosed in European patent application 0347146;
 - vi a condensed pyrimidine derivative as disclosed in European patent application 0349239;
 - vii a pyrimidopyrimidine derivative as disclosed in European patent application 0351058;
 - viii a purine compound as disclosed in European patent application 0352960;
 - ix a quinazolinone derivative as disclosed in European patent application 0371731;
 - x a phenylpyrimidone derivative as disclosed in European patent application 0395328;
 - xi an imidazoquinoxalinone derivative or its aza analogue as disclosed in European patent application 0400583;
 - xii a phenylpyrimidone derivative as disclosed in European patent application 0400799;
 - xiii a phenylpyridone derivative as disclosed in European patent application 0428268;

- xiv a pyrimidopyrimidine derivative as disclosed in European patent 0442204;
 - xv a 4-aminoquinazoline derivative as disclosed in European patent application 0579496;
 - xvi a 4,5-dihydro-4-oxo-pyrrolo[1,2-a]quinoxaline derivative or its aza analogue as disclosed in European patent application 0584487;
 - xvii a polycyclic guanine derivative as disclosed in International patent application WO91/19717;
 - xviii a nitrogenous heterocyclic compound as disclosed in International patent application WO93/07124;
 - xix a 2-benzyl-polycyclic guanine derivative as disclosed in International patent application WO 94/19351;
 - xx a quinazoline derivative as disclosed in US patent 4060615
 - xxi a 6-heterocyclyl pyrazolo [3,4-d]pyrimidin-4-one as disclosed in US patent 5294612
 - xxii a benzimidazole as disclosed in Japanese patent application 5-222000; or
 - xxiii a cycloheptimidazole as disclosed in European Journal of Pharmacology, 251, (1994), 1.
 - xxiv a N-containing heterocycle as disclosed in International patent application WO94/22855.
2. The use of a compound as claimed in claim 1 wherein said compound is:
- a 4-aminoquinazoline derivative as disclosed in European patent application 0579496;
 - a nitrogenous heterocyclic compound as disclosed in International patent application WO93/07124;
 - a 6-heterocyclyl pyrazolo [3,4-d]pyrimidin-4-one as disclosed in US patent 5294612 or
 - a N-containing heterocycle as disclosed in International patent application WO94/22855.
3. The use of a compound as claimed in claim 1 wherein said compound is:
- 1,3-dimethyl-5-benzylpyrazolo[4,3-d]pyrimidine-7-one;
 - 2-(2-propoxyphenyl)-6-purinone;
 - 6-(2-propoxyphenyl)-1,2-dihydro-2-oxopyridine-3-carboxamide;

2-(2-propoxyphenyl)pyrido[2,3-d]pyrimid-4(3H)-one;
 7-methylthio-4-oxo-2-(2-propoxyphenyl)-3,4-dihydropyrimido[4,5-d]pyrimidine;
 6-hydroxy-2-(2-propoxyphenyl)pyrimidine-4-carboxamide;
 1-ethyl-3-methylimidazo[1,5a]quinoxalin-4(5H)-one;
 4-phenylmethylamino-6-chloro-2-(1-imidazoloyl)quinazoline;
 5-ethyl-8-[3-(N-cyclohexyl-N-methylcarbamoyl)-propyloxy]-4,5-dihydro-4-oxo-
 pyrido[3,2-e]pyrrolo[1,2-a]pyrazine;
 5'-methyl-3'-(phenylmethyl)-spiro[cyclopentane-1,7'(8'H)-(3'H)-imidazo[2,1-
 b]purin]4'(5'H)-one
 1-[6-chloro-4-(3,4-methylenedioxybenzyl)aminoquinazolin-2-yl]piperidine-4-
 carboxylic acid;
 (6aR,9aS)-2-(4-trifluoromethylphenyl)methyl-5-methyl-3,4,5,6a,7,8,9,9a-
 octahydrocyclopent[4,5]imidazo[2,1-b]purin-4-one;
 1-tert-butyl-3-phenylmethyl-6-(4-pyridyl)pyrazolo[3,4-d]pyrimid-4-one;
 1-cyclopentyl-3-methyl-6-(4-pyridyl)-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimid-4-one;
 2-butyl-1-(2-chlorobenzyl)6-ethoxycarbonylbenzimidazole;
 2-(4-carboxypiperidino)-4-(3,4-methylenedioxybenzyl)amino-6-nitroquinazoline;
 or 2-phenyl-8-ethoxycycloheptimidazole.

4. The use of a compound as claimed in claim 3 where said compound is:
 4-phenylmethylamino-6-chloro-2-(1-imidazoloyl)quinazoline;
 1-[6-chloro-4-(3,4-methylenedioxybenzyl)aminoquinazolin-2-yl]piperidine-4-
 carboxylic acid;
 (6aR,9aS)-2-(4-trifluoromethylphenyl)methyl-5-methyl-3,4,5,6a,7,8,9,9a-
 octahydrocyclopent[4,5]imidazo[2,1-b]purin-4-one;
 1-tert-butyl-3-phenylmethyl-6-(4-pyridyl)pyrazolo[3,4-d]pyrimid-4-one;
 1-cyclopentyl-3-methyl-6-(4-pyridyl)-4,5-dihydro-1H-pyrazolo[3,4-d]pyrimid-4-one;
 or
 2-(4-carboxypiperidino)-4-(3,4-methylenedioxybenzyl)amino-6-nitroquinazoline;

5. The use of a compound which is a selective cGMP PDE inhibitor for the manufacture of a medicament for the treatment of erectile dysfunction in a male animal, including man, wherein said compound is:

xxv a pyrazolopyrimidine derivative as disclosed in European patent application 0636626;

xxvi a 4-aminopyrimidine derivative as disclosed in European patent application 0640599;

xxvii a imidazoquinazoline derivative as disclosed in International patent application WO95/06648;

xxviii an anthranilic acid derivative as disclosed in International patent application WO95/18097;

xxix a 4-aminoquinazoline derivative as disclosed in US patent 5436233;

xxx a tetracyclic derivative as disclosed in International patent application WO95/19978;

xxxi a imidazoquinazoline derivative as disclosed in European patent application 0668280; or

xxxii a quinazoline compound as disclosed in European patent application 0669324.

6. The use of a compound which is a selective cGMP PDE inhibitor for the manufacture of a medicament for the curative or prophylactic treatment of female sexual dysfunction, premature labour or dysmenorrhea, wherein said compound is a compound as previously claimed in any one of claims 1 to 5 for use in the treatment of erectile dysfunction in a male.

7. A method for the treatment of erectile dysfunction in a male animal or female sexual dysfunction, premature labour or dysmenorrhea, which comprises administering an effective amount of a compound which is a selective cGMP PDE inhibitor as previously claimed in any one of claims 1 to 5.

ABSTRACT

cGMP-PDE INHIBITORS FOR THE
TREATMENT OF ERECTILE DYSFUNCTION

Pyrazolopyrimidine compounds which are selective inhibitors of cGMP PDE are useful in the treatment of erectile dysfunction (impotence) in male animals, including man.